UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,057	07/11/2001	K. Roger Aoki	16952CON1DIV8DIV5	3069

7590 12/24/2003

Stephen Donovan
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612

EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,057	AOKI ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response of the paper filed September 30, 2003 is acknowledged. Claims 21-30 have been cancelled. Claim 31 is pending. The following action includes new references, not necessitated by amendment. The action is therefore made non-final.

35 U.S.C. § 103 Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Arnon (US 5562907) in view of Borodic et al. (1993, Ophthal Plast Reconstr Surg) or Schantz et al. (1992, Microbiological Reviews) or Wilson et al. (1982; Pediatr Infect Dis).

Arnon teaches that "the properties of botulinal toxins have allowed them to be used therapeutically. Botulinum toxin [i.e. type B] is used to produce a temporary muscle paralysis in diseases characterized by: 1) overactivity of a particular muscle or muscle group (e.g., strabismus)" (col 1, ¶ 4 to col. 2, top). Botulinum toxin has "accepted usage for treatment of strabismus and various dystonias" (col. 7, lines 5-6). "These different toxin types have arbitrarily been assigned the letters A through G. *[All] [b]otulinum toxin produces muscle paralysis and relaxation by blocking the motoneuron from releasing acetylcholine at the neuromuscular junction. This effect derives from the enzymatic action of the "light" (50,000 MW) chain of botulinum toxin, the various types (A-G)* of which hydrolyze key proteins which the

motoneuron relies on for the release of the acetylcholine-containing vesicles that trigger muscle contraction." (col. 1, ¶ 3; alteration in original, emphasis added). Further:

> *Numerous therapeutic uses for botulinum toxin were addressed at a November 1990 National Institutes of Health Consensus Development conference. The consensus panel from this conference resolved that botulinum toxin therapy is safe and effective for treating strabismus*, blepharospasm, hemifacial spasm, adductor spasmodic dysphonia, jaw-closing oromandibular dystonia, and cervical dystonia. (Clinical Use of Botulinum Toxin. (Reprinted from NIH Conses. Dev. Conf. Consens. Statement 1990 Nov 12-14; 8(8)) Because the effects of the toxin last for only a few months, repeated injections of toxin are necessary to sustain its therapeutic benefit for chronic conditions. (col. 2, ¶1; emphasis added).

[Note: Although column 2, ¶ 2 of Arnon states that only botulinum type A toxin has been *approved* by the FDA (as of December 1989), it is clear that all botulinum toxins exhibit the same affect muscle paralysis effects on strabismus, as evidenced by the previous two paragraphs of columns 1 and 2 and the 1990 NIH consensus panel general reference to all "botulinum toxins" for treating i.e. strabismus; irregardless of whether the other botulinum strains were approved by the FDA prior to Applicant's filing date]. Arnon does not expressly teach the "administering" step (though intrinsic in the references as taught by "injection" and "therapy" (col. 2, ¶ 1)).

As discussed in the previous action, Borodic et al. teach botulinum B toxin as an alternative to botulinum A toxin since type B produces pharmacologic effects on innervation of striated muscle similar to type A (abstract, as cited in IDS, Paper No. 5). More importantly, Borodic et al. teach that immunologic tolerance has been demonstrated after therapeutic botulinum A toxin injections, implicating type B as a likely candidate for replacement therapy in those who have developed immunologic tolerance to type A (abstract).

As discussed in the previous action, Schantz et al., like Borodic et al., also teach that "[t]ypes of botulinum [i.e. B] other than type A toxin . . . may be useful for human treatment if patients develop immunity to type A toxin (page 93, "Conclusion", last ¶; as cited in IDS, Paper No. 5).

As discussed in the previous action, Wilson et al. teach that "extraocular muscle paralysis, dilated pupils . . . occurred significantly more frequently among infants with type B botulism than among those with type A botulism" (abstract), indicating that type B would likely serve to reduce muscle spasm with greater potency than type A, if used for such treatments.

If not apparent from the teachings of Arnon, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use botulinum type B as taught by any of Borodic et al., Schantz et al., or Wilson et al., to treat strabismus in the method of treatment using any botulinum toxin, including type B, of Arnon; because either Borodic et al. or Schantz et al. teach that it would be advantageous to use botulinum type B in the treatment of muscle fibers (i.e. spasms such as blepharospasm and/or strabismus) when type A immunologic tolerance has developed in a patient; or because Borodic et al. teach that type B may work as effectively on striated muscle as type B (wherein shortages or impurities of type A would warrant the use of type B); or because Wilson et al. teach that clinical results in humans show that type B can reduce muscle spasm with greater potency than type A; and because Arnon teaches the advantageous use of any botulinum toxin may be used to treat strabismus, including type B.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Graham (US 2002/0102275 A1), in view of any of Arnon (US 5562907) Borodic et al. (1993, Ophthal Plast Reconstr Surg) or Schantz et al. (1992, Microbiological Reviews) or Wilson et al. (1982; Pediatr Infect Dis).

Graham teach the use of botulinum type A for the treatment of strabismus and also contemplates the use of other botulinum toxins, including type B (¶'s 0008 and 0007, and claims 4 and 7). Graham does not expressly teach the use of type B for treating strabismus.

Arnon, Borodic et al., Schantz et al, and Wilson et al. are all discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use botulinum type B as taught by any of Arnon, Borodic et al., Schantz et al., or Wilson et al., to treat strabismus in the method of treatment using botulinum type A of Graham; because Arnon teaches the advantageous use of any botulinum toxin may be used to treat strabismus, including type B; and either Borodic et al. or Schantz et al. teach that it would be advantageous to use botulinum type B in the treatment of muscle fibers (i.e. spasms such as blepharospasm and/or strabismus) when type A immunologic tolerance has developed in a patient; or because Borodic et al. teach that type B may work as effectively on striated muscle as type B (wherein shortages or impurities of type A would warrant the use of type B); or because Wilson et al. teach that clinical results in humans show that type B can reduce muscle spasm

with greater potency than type A; and because Graham teaches the use of botulinum type A for treating strabismus and contemplates the use of other toxins, such as type B.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection of claim 31 under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. (US 5696077) in view of Elston et al. (1985, Br J Opthalmol); further in view of Borodic et al. (1993, Ophthal Plast Reconstr Surg) or Schantz et al. (1992, Microbiological Reviews) or Wilson et al. (1982; Pediatr Infect Dis), is maintained for the reasons of record. Applicant has presented no arguments for why claim 31 is patentable over the above rejection.

The rejection of claim 31 is also herein rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al. in view of Arnon (US 5562907).

As discussed in the previous action, Johnson et al. teach the use of botulinum type B for muscle spasms, namely:

> A method for treating movement disorders characterized by uncontrolled muscle spasm using the pharmaceutical preparation is also the subject of the present invention. The treatment involves parenteral local administration of an effective dose of the present preparation directly to the afflicted muscle or muscles. The neurotoxin complex temporarily interrupts or lessens the neural connection between the muscle and nerve endings, thereby relieving the involuntary contraction of the muscle. *Disorders which can be treated using the present preparation* ***include, for example,*** *blepharospasm, hemifacial spasm, spasmodic torticollis, spasmodic dysphonia, regional hand dystonias, and muscle hypertrophy.* (col. 2, last ¶ to col. 3, 1st ¶; emphasis added; see also col. 1, lines 42-47).

Although strabismus is also a well-known muscle spasm disorder, Johnson et al. does not expressly have it listed in the unclosed list of examples of muscle spasm disorders.

Arnon is discussed above and expressly teaches the use of botulinum toxins, including botulinum type B, for the treatment of strabismus.

As discussed in the previous action, Elston et al. teach successful treatment of strabismus with Botulinum toxin type A by injection (abstract; and as cited in US 6290961 at column 1, lines 42-43).

Borodic et al., Schantz et al., and Wilson et al. are all discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use botulinum type B as taught by Arnon, Borodic et al., Schantz et al., or Wilson et al., further in view of Elston et al., to treat *strabismus* in the method of treatment using botulinum type B of Johnson et al.; because Arnon expressly teaches the advantageous use of any botulinum toxin, including type B for strabismus, and Borodic et al. or Schantz et al. teach that it would be advantageous to use botulinum type B in the treatment of muscle fibers (i.e. spasms such as blepharospasm and/or strabismus) when type A immunologic tolerance has developed in a patient; or because Borodic et al. teach that type B may work as effectively on striated muscle as type B (wherein shortages or impurities of type A would warrant the use of type B); or because Wilson et al. teach that clinical results in humans show that type B can reduce muscle spasm with greater potency than type A; and further in view of Elston et al.'s likewise treatment of strabismus, another type of "muscle spasm" with botulinum type A. Additionally, because Johnson et al. teach that botulinum type B may be use to treat any muscle spasm, and has not limited by example or excluded other well known muscle spasm disorders

such as strabismus, which is clearly contemplated by Johnson et al. use of an unclosed list of muscle spasm disorder examples capable of treatment with botulinum type B.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection of claim 31 under 35 U.S.C. 103(a) as being unpatentable over Elston et al. (1985, Br J Opthalmol) in view of Borodic et al. (1993, Ophthal Plast Reconstr Surg) or Schantz et al. (1992, Microbiological Reviews) or Wilson et al. (1982; Pediatr Infect Dis), is maintained for the reasons of record. Applicant has presented no arguments for why claim 31 is patentable over the above rejection.

The rejection of claim 31 is also herein rejected under 35 U.S.C. 103(a) as being unpatentable over Elston et al. in view of Arnon (US 5562907).

As discussed in the previous action, Elston et al. teach successful treatment of strabismus with Botulinum toxin type A by injection (abstract; and as cited in US 6290961 at column 1, lines 42-43). Elston et al. does not expressly teach the use of type B to treat strabismus.

Arnon, Borodic et al. (1993, Ophthal Plast Reconstr Surg), Schantz et al. (1992, Microbiological Reviews), and Wilson et al. (1982; Pediatr Infect Dis) are all discussed above.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use botulinum type B as taught by any of Arnon, Borodic et al., Schantz

et al., or Wilson et al., to treat strabismus of Elston et al.; because Arnon expressly teaches the advantageous use of any botulinum toxin, including type B, to treat strabismus, and either Borodic et al. or Schantz et al. teach that it would be advantageous to use botulinum type B in the treatment of muscle fibers (i.e. spasms such as blepharospasm and/or strabismus) when type A immunologic tolerance has developed in a patient; or because Borodic et al. teach that type B may work as effectively on striated muscle as type B (wherein shortages or impurities of type A would warrant the use of type B); or because Wilson et al. teach that clinical results in humans show that type B can reduce muscle spasm with greater potency than type A; and because Elston et al. teach the use of advantageous use of type A to treat strabismus.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
December 20, 2003

CHRISTOPHER R. TATE
PRIMARY EXAMINER